REMARKS

Status of the Claims

Claims 17-29 are currently pending. In the present Response, claims 17-22, 28, and 29 are amended; claims 30-43 are added. Thus, after entry of these amendments, claims 17-43 are presented for consideration.

Pursuant to the Office Action, claims 17-27 are rejected under 35 U.S.C. §112, first paragraph. Claims 18, 28, and 29 are rejected under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse all outstanding rejections of the claims.

Support for Claim Amendments

Support for claim amendments can be found throughout the specification. In particular, support for amendments to claims 28 and 29 and new claims 30-43 directed to enzymes having at least 70% sequence identity and the stated activity can be found at least at page 13, lines 17-24; and page 14, lines 22-27. The amendment to claims 17-22 merely clarify the claimed invention. Applicants respectfully submit that no new matter is introduced by the instant amendments.

Issues under 35 U.S.C. §112, first paragraph

Claims 17-27 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Patent Office alleges that transaminase or aminotransferase encompasses diverse enzymes having any substrate and stereo specificity. While the claims impart a structural limitation (70, 80, 90, or 95%), there is no specific functional limitation.[1]

[1] See page 2, line 21, to page 3, line 2, of the Office Action.

Thus, it is alleged that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree. It should be noted that the level of knowledge and experience of the skilled artisan was very high at the time the application was filed. Thus, the skilled artisan would understand that transaminases or aminotransferases are enzymes that can transfer a nitrogenous group from a donor to an acceptor such as catalyzing the transfer of an amino group from an amino acid to an α-keto acid. Therefore, the skilled artisan would understand that the enzymes will require an amino acid and an α-keto acid as substrates, both of which the skilled artisan would recognize. The skilled artisan would also understand that to be an enzyme of the invention, structurally, it must be at least 70% identical to the amino acid sequences of SEQ ID NOS:25-32 and, functionally, it must have transaminase or aminotransferase activity, new claims 30-43 describe that claimed invention with more particularity.

Applicants have named eight representative aminotransferases to describe the genus. The scope of the claimed invention, however, does not encompass just any enzymes, only those that have aminotransferase activity and that have at least 70% sequence identity to SEQ ID NOS:25-32.

Therefore, to limit the broad claims to a specific transaminase or aminotransferase for specific substrates would provide too narrow a coverage and would allow potential infringers to use the teachings of the instant application to devise polynucleotides that encode an amino acid sequence related to SEQ ID NOS:25-32, but that have different donor or acceptor specificity. Like many, if not all enzymes, the aminotransferases of SEQ ID NOS:25-32 catalyze reactions to attain specific products from specific reactants. In other words, the catalytic reaction will be dependent on the specific reactants; however, the action/activity will remain the same. It would, therefore, be onerous for the Applicants to list every possible reaction that the enzymes may catalyze and unnecessary for the skilled artisan to practice the claimed invention.

Applicants, in a previous response, provided examples of issued claims where the USPTO found percent sequence homology/identity and a general activity sufficient to describe the claimed invention. In response the Patent Office stated it would be improper for the examiner to review the file wrapper of the issued application for the purpose of answering the arguments in the unrelated case. Applicants submit that the exemplary issued claims were cited merely for the proposition that in general such claim language has been found to be acceptable to the Patent Office, *i.e.*, where a polypeptide is claimed in terms of its activity, *e.g.*, DNA polymerase, without reference to a particular species of the enzymes having this activity or its specific substrates.

For the reasons provided above, Applicants respectfully submit that the written description requirement under 35 U.S.C. §112, first paragraph, has been met for the claimed invention, namely, the claimed invention is sufficiently described in terms of a structural limitation and a functional limitation related to the activity of the enzyme.

Based on the teachings of the instant disclosure, the skilled artisan would know that enzymes of the invention would have at least 70% identity to the amino acid sequences of SEQ ID NOS:25-32 and that the enzymes must have transaminase or aminotransferase activity. Accordingly, the claimed invention is described in terms of its structure and its function.

Moreover, it is well within the knowledge of the skilled artisan to introduce mutations in proteins and to isolate DNA molecules (such as by library screening) encoding variant enzymes that fall within the scope of the claims. Once these variants are isolated, it is within the knowledge of the skilled artisan to identify those enzymes whose amino acid sequence is within the scope of the claimed invention (*e.g.*, at least 70% identical when aligned by BLASTP). It is also within the knowledge of the skilled artisan to identify those enzymes whose function is that of a transaminase or aminotransferase, such as transferring an α-amino group from one amino acid to an α-ketoglutarate, as acknowledged by the Patent Office on page 6, line 19, to page 20, line 1, of the Office Action. These activities would be a matter of routine experimentation (*e.g.*,

sequencing the new clone and using the alignment program of BLASTP to measure percent identity and then using known methods to test the enzyme for its ability to transfer amino groups).

Regarding the difference between routine experimentation and undue experimentation, the Federal Circuit in *In re Wands* directed that the focus of the enablement inquiry to be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" is set forth by the Federal Circuit in, *e.g.*, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*[2] An applicant had claims that were generic to all IgM antibodies directed to a specific antigen. However, only a single antibody producing cell line had been deposited.[3] The PTO had rejected claims that were generic to all antibodies directed to the antigen as lacking an enabling disclosure.

The Federal Circuit reversed, noting that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody species was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

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[2] *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

[3] The cell line was a hybridoma, thus, all of the antibodies it produced had the same structure and activity.

Analogously, it would not be undue experimentation to screen libraries or create mutations based upon the sequences taught in the instant specification to arrive at Applicants' claimed invention, as these protocols are well known, well accepted and practiced every day in research laboratories. Therefore, in light of the reasons provided above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as applied to claims 17-29.

In the Patent Office's response to Applicants' arguments, it alleged "the genus of transaminases encompasses enzymes with widely different functions and because of that, a functional characteristic such as "transaminase activity is insufficient."[4]

Applicants aver that a limitation of Applicants' claimed invention is that the enzymes must have transaminase or aminotransferase activity. This activity (function) is described in the application as the transfer of an amino group from an amino acid to an α-keto acid. In other words, all enzymes of the claimed invention must have transaminase or aminotransferase activity. Accordingly, Applicants respectfully submit that one skilled in the art would have appreciated the scope of the claimed invention.

With regard to the enablement argument, the Patent Office agrees that one of skill in the art would have known how to determine a specific defined transaminase activity, but disagrees with the notion that one skilled in the art would have known how to determine any possible transaminase or aminotransferase activity.[5] Applicants respectfully submit that one skilled in the art would have been able to determine the transaminase or aminotransferase activity of an enzyme, *i.e.*, transferring an amino group from an amino acid to an α-keto acid, as exemplified by the transfer of an α-amino group to the α-carbon atom of α-ketoglutarate as taught in the specification. Such assays were known in the art at the time the application was filed. Therefore, Applicants respectfully submit that instant claims are sufficiently describe and enable one skilled in the art to

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4 See page 6, lines 12-14, of the Office Action.

5 See page 6, line 19, to page 7, line 7, of the Office Action.

practice the full scope of the claims. Applicants request reconsideration and withdrawal of the rejection of the claims based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §112, second paragraph

Claims 18, 28, and 29 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 18, line 4, recites "an enzyme encoded by an amino acid sequence." Applicants have amended claim 18 to recite "an enzyme that has an amino acid sequence."

Claims 28 and 29 recite "enzyme has the same amino group acceptor and amino group donor specificity" without pointing out and distinctly claiming the amino group acceptor and donor. Applicants have amended these claims, thereby obviating this rejection.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection based under 35 U.S.C. §112, second paragraph, as applied to claims 18, 28, and 29.

CONCLUSION

Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

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